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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,010	08/09/2006	Kenichiro Kosai	55801-002US1	9188

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EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
11/26/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

INFO@ORTPATENT.COM

Office Action Summary	Application No.	Applicant(s)	
	10/567,010	KOSAI ET AL.	
	Examiner	Art Unit	
	Michael Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/31/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 10/4/2010 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18, 23 and 26 recite the limitation "the protein-coding gene"" in line 9 of claim 18, for example. There is insufficient antecedent basis for this limitation in the claim. This rejection affects all dependent claims.

Claims 18, 23 and 26 all recite a step of preparing a "restriction enzyme-recognizing unit" (e.g. lines 3-4 of claim 18) that apparently includes, *inter alia*, two distinct "restriction enzyme-recognizing sequences" that have replaced the endogenous E1A and E1B promoters (e.g. lines 7-11 of claim 18). The next step recited in all the claims is that of introducing a promoter "in the restriction enzyme-recognizing unit" (e.g. lines 12-13 of claim 18). The very nature of a "restriction enzyme-recognizing unit" and a "restriction enzyme-recognizing sequence" renders the terms synonymous, i.e. both encompass the nucleotide sequence (e.g. a 4, 6, or more, stretch of nucleotides with a defined sequence) recognized by a given restriction enzyme that cleaves the

nucleotide sequence (GAATTC is recognized by EcoRI, etc.). Thus it is unclear into which of the three restriction sites or sequences recited in the claims the promoter is to be introduced into. It would be remedial, for example, to term the "restriction enzyme-recognizing unit" an "expression cassette" as this appears to be what is intended by the specification, i.e. an adenoviral E1 expression cassette wherein E1 expression is driven by heterologous promoters. Furthermore, it appears that both E1A and E1B must have a promoter in this invention as their respective endogenous promoters have been removed, thus, reciting that only a single promoter is introduced creates further confusion as to which E1 gene (E1A or E1B) has received the heterologous promoter. It would be remedial, for example, to recite that a promoter has been inserted into both of the restriction enzyme-recognizing sequences recited in the claims (this is the situation presented in the Figures of the instant specification). This rejection affects all dependent claims.

Claim 26 is unclear for not reciting a positive process step that refers back to the preamble of the claim. The claim recites, in the preamble, that it is a method for "preparing a proliferation-regulated recombinant adenoviral vector having an integrated therapeutic gene". However, the claim provides no method steps for preparing such an adenoviral vector, rather, the claim stops after method steps for preparing what appear to be precursors for such an adenoviral vector. That is, the claimed method stops after preparing a sequence comprising an adenoviral E1 expression cassette followed by a therapeutic gene. Given the accepted meaning of a "proliferation-regulated adenoviral vector" in the prior art and instant specification as a conditionally replicating adenovirus, the DNA sequence prepared by the method steps in this claim fall far short of such an adenoviral vector. What is required is a step as recited in claims

18 or 23 wherein the modified E1 region or therapeutic gene are inserted into an E1-deleted adenoviral genome. It would be remedial to remove or amend the preamble to be inline with the active method steps recited in the claim; or to add a method step to provide for the product recited in the preamble (although the latter would render the claim very similar in scope to claim 23).

The term "high-expression" in claims 23 and 26 is a relative term which renders the claims indefinite. The term " high-expression" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Objections

Claims 18, 23 and 26 are objected to because of the following informalities: "in a target organ in the restriction enzyme-recognizing unit" should be "in a target organ into the restriction enzyme-recognizing unit". Appropriate correction is required.

Claims 26 is objected to because of the following informalities: "preparing a proliferation-regulated adenoviral plasmid by (i) preparing a proliferation-regulated plasmid by preparing..." is both clumsy and confusing language. Appropriate correction is required.

Double Patenting

Applicant is advised that should claims 18, 23 or 26 be found allowable, claims 20, 25, 28, 34 and 37 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The dependent claims merely recite all possible situations of E1B expression already found in the parent claims. This is because the E1B region of adenoviruses contains only the E1B-19K and E1B-55K coding regions.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Nagano et al (2005) appears to be a publication of the work found in the instant application. Hardy et al (1997) detail methods to modify E1-deleted adenoviral vectors by insertion of heterologous genes into the E1 region using a recombinase-based system. See Figs. 1 and 3 in particular. However, Hardy et al do not teach the E1 expression cassette of the instant claims, but rather are focused on vectors devoid of E1 altogether (typical of gene therapy applications of adenovirus). WO 01/73093 teaches several iterations of E1 expression cassettes wherein the endogenous E1 promoters are replaced with various substitutes in order to prepare conditionally replicating adenovirus vectors, however, this reference does not teach the use of a recombinase site or the recombinase itself. The vectors in WO 01/73093 were prepared using the classical techniques of adenoviral manipulation: ligation and homologous recombination (see Example 1 in particular).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/
Primary Examiner, Art Unit 1633